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MEDICAL TUBE FOR ASEPTIC CONNECTION

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[There are no amendments to this patent.]

Abstract

Constitution

To provide a medical tube for aseptic connection made of a thermoplastic polyester with a glass-transition temperature of 0°C or lower.

Effect

The medical tube is the optimum choice for aseptic connection because of its good performance as well as excellent productivity and safety.

Claim

A medical tube for aseptic connection made of a thermoplastic polyester with a glass-transition temperature of 0°C or lower.

Detailed explanation of the invention

[0001]

Industrial application field

The present invention pertains to a type of tube (connecting tube) used for transporting blood, infusion agent, or other liquid handled in the medical field.

[0002]

Prior art and problems to be solved by the invention

In addition to safety, hygienic standards, softness, transparency, heat resistance, and other general properties, it has been required recently that the material of a tube used for blood sampling, blood transfusion, infusion, or other medical activities be able to prevent microbes from entering the tube from the outside and be applicable to the so-called "aseptic connection," that is, connection between two tubes. For example, as described in Japanese Kokoku Patent No. Sho 61[1986]-30582, said aseptic connection is "a method for connecting a first and a second thermoplastic tube in a direction that crosses the axis of each tube. A cutting means with a heated cutting surface is used to cut the tubes, and a continuous melt seal is formed between the heated cutting surface and the cross section of each tube. In this way, the seal can be retained between each tube and the outside. While the melted end portions of the tubes are connected to each other

and kept in a sealed state, connection can be realized between the tubes." In other words, the tubes that can be used in this system must be made of a thermoplastic polymer, and the adhesion strength of the formed connection part (connection becomes a "butt connection" state) must be practically high.

[0003]

Since the most commonly used medical tube made of soft polyvinyl chloride satisfies the aforementioned requirements, soft polyvinyl chloride naturally becomes the material used exclusively for the aforementioned system. However, there is a demand on making a transfer to other materials because soft polyvinyl chloride has problems concerning poor resistance to low temperature, elution of plasticizer, and waste disposal. On the other hand, soft polyvinyl chloride has been used widely because of its good properties, including softness, transparency, and heat resistance. Consequently, it is required to develop a type of tube "which is made of a non-polyvinyl chloride type material and can be aseptically connected to a tube made of polyvinyl chloride" (needless to say, the tubes made of a non-polyvinyl chloride material should also be able to be connected to each other). However, most materials cannot be used for medical tubes for aseptic connection because they do not satisfy the aforementioned requirement.

[0004]

Means to solve the problems

In order to solve the aforementioned problem, the present inventors have performed extensive research with the purpose of providing types of tubes which are made of a non-polyvinyl chloride type material and can be connected not only to each other but also to polyvinyl chloride tubes. As a result of this research work, it was found that a tube made of a thermoplastic polyester with a glass-transition temperature (hereinafter abbreviated T_g) of 0°C or lower can realize the aforementioned purpose. The present invention was achieved based on the aforementioned research.

[0005]

The thermoplastic polyester mentioned in the present invention refers to a polymer which is made of the well-known linear polyester constituent components and has a T_g of 0°C or lower. The thermoplastic polyester is usually manufactured by combining the following compounds in an appropriate manner so that the glass-transition temperature of the generated polyester is 0°C or lower, followed by esterification (ester interchange), copolymerization, etc., performed using the conventional methods. The aforementioned compounds include malonic acid, succinic acid, adipic acid, pimelic acid, suberic acid, azelaic acid, sebacic acid, dodecandioic acid, dimer acid

(preferably, hydrogenated product), terephthalic acid, isophthalic acid, sodium-5-sulfoisophthalic acid, naphthalenedicarboxylic acid, and other low-molecular dicarboxylic acids and their alkyl esters, ethylene glycol, trimethylene glycol, propylene glycol, 1,4-butanediol, neopentyl glycol, 1,5-pentanediol, 1,6-hexanediol, 1,7-heptanediol, 1,8-octanediol, 1,9-nonanediol, 1,10-decanediol, diethylene glycol, triethylene glycol, 1,4-cyclohexanedimethanol, 2,2-bis(p-β-hydroxyethylphenyl)propane, bis(p-β-hydroxyethylphenyl)sulfone, and other low-molecular glycols, ε-hydroxycaproic acid and other low-molecular oxy acids, ε-caprolactone and other low-molecular lactones, polyethylene oxide, polypropylene oxide, ethylene oxide-propylene oxide copolymer, polytetramethylene oxide (polytetrahydrofuran), and other polyethers having ester-forming functional groups (such as carboxyl groups, alkoxycarboxyl groups, hydroxyl groups) at the terminals. Generally speaking, the amount of hard segments is increased along with the increase in the content of the aromatic component (decrease in the aliphatic component). As a result, T_g becomes higher. Introduction of a polyether or other soft component is very effective in lowering T_g (a polyether with a number-average molecular weight in the range of 500-10,000, preferably in the range of 800-8,000 is recommended because a homogeneous polyester can be obtained). It is also possible to add a compound having three or more functional groups, such as trimellitic acid, trimesic acid, trimethylolpropane, or pentaerythritol, as long as the "thermoplastic property" is not affected.

[0006]

The T_g of the polyester used as the tube material in the present invention must be 0°C or lower. If the T_g of the polyester is higher than 0°C, a good connection surface cannot be formed during aseptic connection. In particular, a sufficiently high adhesion strength cannot be obtained during aseptic connection to a soft polyvinyl chloride tube (because the compatibility with polyvinyl chloride becomes low), and the resistance to low temperature is also degraded. However, the T_g is preferred to be -20°C or lower in consideration of the softness of the tube itself. Also, as far as the moldability and strength are concerned, the intrinsic viscosity of the polyester used for forming the tube measured at 25°C in an equiweight solvent mixture of phenol/sym-tetrachloroethane should be in the range of 0.4-5.0, or preferably in the range of 0.5-4.0.

[0007]

The tube of the present invention is manufactured using the conventional melt extrusion method. The melting temperature is preferred to be in the range of 10-50°C higher than the incipient fluidization temperature (usually in the range of 80-200°C) of the thermoplastic polyester. Although they vary depending on the application, the tube usually has a circular cross

section, an outer diameter in the range of 2-10 mm, and a thickness in the range of 0.3-2 mm. It is also possible to add a heat resistance agent, weather resistance agent, pigment, etc., as long as the main point of the present invention are not affected.

[0008]

The medical tube of the present invention includes (a) a tube made of a polymer composition consisting of a polyester with a low T_g mentioned in the present invention and another polymer, such as a polyester with a high T_g (T_g is higher than 0°C), polyvinyl chloride, vinyl chloride-ethylene-vinyl acetate copolymer, or vinyl chloride-urethane copolymer, (b) a multilayer tube made of a polyester with a low T_g mentioned in the present invention and another polymer (for example, a two-layer or three-layer tube with the inner layer, intermediate layer, or outer layer made of the polyester with a low T_g mentioned in the present invention and with the inner layer and/or outer layer made of a polyester with a high T_g), (c) a tube made of a composition consisting of two or more types of the polyesters with low T_g mentioned in the present invention, and (d) a multilayer "aseptically connectable" tube made of two or more types of the polyesters with low T_g mentioned in the present invention.

[0009]

In order to prevent blocking during processing or use and to improve the operability, the inner or outer surface of the tube can be roughened (embossed), and a blocking inhibitor/slipping agent can be added.

[0010]

Also, examples of the tubes that can be aseptically connected to the tube of the present invention (the matching tube) include (A) the tube of the present invention, (B) a polyvinyl chloride tube, such as a tube made of polyvinyl chloride containing di-2-ethylhexylphthalate, di-n-decylphthalate, tri-2-ethylhexyltrimellitate, butyryltri-n-hexylcitrate, or polyester as a plasticizer, ethylene vinyl acetate copolymer-modified polyvinyl chloride, or polyurethane-modified polyvinyl chloride, and (C) a tube made of a polyester with a high T_g (T_g higher than 0°C).

[0011]

The medical tube of the present invention can be used to transport blood or its constituents, culture medium, buffer, infusion agent, peritoneal dialyzate, etc.

[0012]

Application examples

In the following, this invention will be explained in more detail with reference to application examples.

[0013]

(1) Experimental methods

(1) Synthesis of polyester

Dimethyl adipate, dimethyl terephthalate, ethylene glycol, 1,4-butanediol, and polytetramethylene oxide with a molecular weight of 2000 and having hydroxyl groups at the two terminals were added in appropriate amounts into a polymerization container equipped with a stirrer. After tetra-n-butyltitanate was added in an amount of 0.2×10^{-4} mol with respect to 1 mol of the dicarboxylic acid components, ester interchange was carried out at a temperature in the range of 150-200°C under normal pressure for 3-4 h. Then, the pressure in the system was gradually reduced to 0.1 torr within 1 h. After that, polycondensation was carried out at 230°C for 2.5-3.5 h, obtaining polyesters with various compositions.

[0014]

(2) Evaluation of the properties of the polyester

A Ubbelohde viscometer was used to measure the intrinsic viscosity (η) at 25°C in an equiweight solvent mixture of phenol/sym-tetrachloroethane. Also, T_g was measured at a heating rate of 10°C/min using a DSC3100 differential scanning calorimeter produced by Mark Science Co.

[0015]

(3) Molding of polyester tube

Polyester was melted at a temperature in the range of 210-220°C and extruded from a tube die to obtain a tube with an inner diameter of 3.0 mmΦ and an outer diameter of 4.4 mmΦ.

[0016]

(4) Aseptic connection test

A "butt connection" test was carried out for (A) polyester tubes and (B) a polyester tube and a soft polyvinyl chloride tube (containing 55 phr of di-2-ethylhexylphthalate and having the same diameter as the polyester tube) using an SCD (aseptic connection apparatus) produced by DuPont Co. under the following conditions: wafer temperature: 240-300°C, time: 10-20 sec. The connection strength of the obtained connected tube was measured with a tensile tester (the

connection strength listed in Table 1 is the maximum connection strength of the connected tube obtained under the aforementioned conditions).

[0017]

(5) Safety test

A "test for plastic container for infusion" was carried out using the general test method described in the 12th revised Japanese pharmacopoeia for the polyester tube molded using the aforementioned method.

[0018]

(2) Experimental results

Table 1 lists the experimental results. All of the synthesized polyesters can be molded into tubes under the aforementioned conditions.

[0019]

The polyester tubes with low T_g show practical connectability not only between the polyester tubes themselves but also in the connection with polyvinyl chloride tubes.

[0020]

Also, all of the polyester tubes passed the "test for plastic container for infusion" described in the Japanese pharmacopoeia.

[0021]

Table 1

	1 ポリエステル組成(モル%)	2 物性		3 接合強度(kg)		6 安全性
	ADA/TPA//EG/BD/PTMO	[η]	Tg(℃)	4 (イ)	5 (ロ)	
8 実施例1	30/70//30/70/0	0.8	-3	3.6	3.0	合格
実施例2	30/70//30/69/1	1.0	-10	5.7	3.2	合格
実施例3	30/70//27/67/6	1.2	-40	6.2	3.7	合格
実施例4	30/70//25/65/10	1.4	-65	6.7	4.2	合格
実施例5	30/70//20/60/20	1.9	-85	7.1	4.0	合格
9 比較例1	25/75//30/70/0	0.8	5	0.7	0.2	合格
10 参考例	ポリ塩化ビニルチューブ同士の接合 11	−	−	−	8.4	−

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注1．ポリエステル組成におけるモル%はジカルボン酸成分およびグリコール成分の合計が100モル%となるように表示した。

注2．ADA：アジピン酸成分

TPA：テレフタル酸成分

EG：エチレングリコール成分

BD：1,4,-ブタンジオール成分

PTMO：ポリテトラメチレンオキシド成分

注3．接合強度（イ）：当該ポリエステルチューブ同士の接合

接合強度（ロ）：当該ポリエステルチューブとポリ塩化ビニルチューブとの接合

注4．引張試験においてチューブはいずれも接合面で破断した。

Key: 1 Polyester composition (mol%)

2 Properties

3 Connection strength
4 (A)
5 (B)
6 Safety
7 Qualified
8 Application Example
9 Comparative Example
10 Reference Example
11 Connection between polyvinyl chloride tubes
12 Note 1. For the polyester composition, the mol% is such that the total amount of the dicarboxylic acid components and the glycol components is 100 mol%.
Note 2. ADA: Adipic acid component
TPA: Terephthalic acid component
EG: Ethylene glycol component
BD: 1,4-Butanediol component
PTMO: Polytetramethylene oxide component
Note 3. Connection strength: (A): Connection between the polyester tubes
Connection strength: (B) Connection between a polyester tube and a polyvinyl chloride tube
Note 4. All of the tubes have broken connection surfaces during the tensile test.

[0022]

Effect of the invention

As can be seen from the experimental results listed in the table, the polyester tube of the present invention shows good performance in aseptic connection and has excellent productivity and safety. Therefore, the polyester tube of the present invention is the optimum choice for a medical tube for aseptic connection.